Appl. No. 10/549,905 Atty. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

Amendments to the Claims

This Listing of Claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended): Conjugates One or more conjugate[[s]] of a polyamine[[s]] with an acidic retinoid[[s]], having pharmaceutical properties; in which [[the]] an R group in a) and/or b) below of the acyl group(s) RCO is one of the retinoid residues R¹-R⁶ set forth in the following acidic retinoids, the retinoid residues obtained by removing the COOH group from each of the following acidic retinoids—and polyene chain shortened all trans retinoic acid analogues:

and said polyamine[[s]] is [[are]]:

a linear tri, tetra-and hexa- polyamine[[s]],
in which case the one or more conjugate[[s]] have has the following general formulae:

Appl. No. 10/549,905

Attv. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

wherein n is 1 to 9; or

[[d)]] b) a branched (dimeric) polyamine[[s]],

in which case the one or more conjugate[[s]]-have has the following general formula:

wherein

R' is COR or (CH₂)₃NHCOR and R" is COR or (CH₂)₃NHCOR and n is one of the numbers 1, 2 or 7.

- (Currently Amended): A method for the preparation of the one or more conjugate a eompound according to claim 1 involving initially step a), followed by step b) or step c):
 - a) synthesis of a compound[[s]] with the general formula

Appl. No. 10/549,905 Attv. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

wherein R is one of the retinoid residues R^1 - R^6 of claim 1, which involves esterification of \underline{an} acidic retinoid[[s]] with $\underline{N-hydroxysuccinimide}$ (HOSu) in the presence of [[the]] \underline{a} coupling agent, which is $\underline{N,N'-dicyclohexylcarbodiimide}$ (DCC) and purification with flash column chromatography to obtain a purified succinimidyl ester[[s]];

- b) direct selective acylation of the primary amino groups functions of the polyamine[[s]] with the purified succinimidyl ester[[s]]; or
- c) selective acylation of the secondary amino groups functions of the polyamine[[s]], protected at their its primary amino functions with a trifluoroacetyl group or a 9-fluorenylmethoxycarbonyl group, with the acidic retinoid[[s]] identified in Fig. 2 of claim 1 in the presence of [[the]] a_coupling agent, which is bromotripyrrolidinophosphonium hexafluorophosphate (PyBrOP), followed by deprotection.
- 3. (Currently Amended): A method according to claim 2, which method involves the direct selective acylation of the primary amino functions of the polyamine[[s]] or their its corresponding hydrochloride or trifluoroacetate salts with the compound[[s]] of the step a) of claim 2, wherein a [[the]] solvent is used which is selected from dichloromethane, chloroform and dimethylformamide[[,]] and the base, where necessary is, is triethylamine or dissopropylethylamine.
- 4. (Currently Amended): A method according to claim 3 wherein the selective acylation of the primary amino functions of the polyamine[[s]] is carried out with any other activated carboxylic acid derivative known to acylate selectively primary amino functions in the presence of secondary amino functions ones.
- 5. (Currently Amended): A method according to claim 2 wherein the selective mono- or bis-acylation of the primary amino functions of the polyamine[[s]] takes place indirectly and involves the following steps:
- [[1.]] (i) protection of the secondary amino functions of the polyamine[[s]], bearing the trityl protecting group at their its primary amino functions, with the 9-fluorenylmethoxycarbonyl group or the trifluoroacetyl group;

[[2]] (ii) detritylation;

Appl. No. 10/549,905 Atty. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

• • •

- [[3]] (iii) mono- or bis-acylation with the compound[[s]] of step a) of claim 2[[;]]
- [[4]] (iv) complete deprotection and purification, if necessary, by flash column chromatography.
- 6. (Currently Amended): A method according to claim 2 wherein the selective acylation of the secondary amino functions of the polyamine[[s]] involves the following steps:
 - (i) selective trifluoroacetylation of the primary amino functions of the polyamine[[s]];
 - (ii) acylation of the secondary amino functions with the acidic retinoids
 - in the presence of the coupling agent PyBroP;
 - (iii) removal of the trifluoroacetyl groups by alkaline hydrolysis.
- (Currently Amended): A pharmaceutical preparation or product containing the one or more conjugate eempounds claimed in claim 1 and a pharmaceutically acceptable carrier for therapeutical applications in humans.
- 8. (New) A method according to claim 3, wherein a base is used which is triethylamine or disopropylethylamine.
- 9. (New) A method according to claim 5, which further involves the following step: [[:]] (iv) complete deprotection and purification by flash column chromatography.